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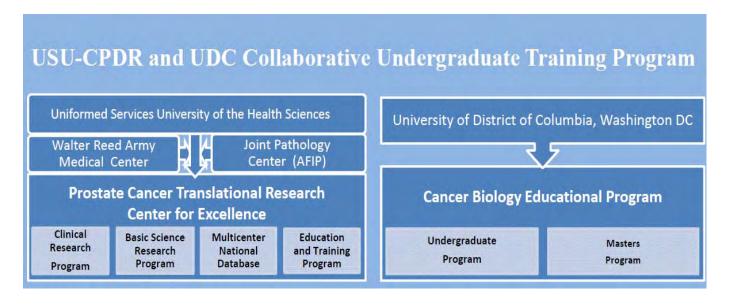
HBCU Summer Undergraduate Training Program in Prostate Cancer Research

INTRODUCTION:

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DISTRICT OF COLUMBIA

The goal of this award was to provide prostate cancer (CaP) research summer internships to the students of the University of the District of Columbia (UDC) at the Uniformed Services University of the Health Sciences (USU)-Center for Prostate Disease Research (CPDR). The main objective was to expose students to stimulating research environment that would encourage them to pursue research or medical careers in prostate cancer or relevant biomedical fields. During this grant period (2008-2010), USU-CPDR and UDC team developed and executed a structured program, offering exciting training opportunities to students in a multi-disciplinary CaP translational research environment of the CPDR. Pioneering research accomplishments and translational research expertise and resources of the CPDR are led by Dr. David G. McLeod (Director) and Dr. Shiv Srivastava (Co-Director), who are established investigators in CaP research. CPDR's mission is to conduct basic science and clinical research programs that strive to combat diseases of the prostate. The integration of basic and clinical science studies is a critical component in improving early detection and prognostic markers and in development of potential treatments for prostate diseases. The CPDR also provides training in molecular biology and clinical research efforts related to prostate disease.



A brief summary of the participating institutions is provided below:

The University of District of Columbia (www.udc.edu) is an HBCU established in 1976 and the nation's only comprehensive urban land-grant institution with the mission of education, research, and public service. Each year, approximately 600 students graduate with an

associate's, a bachelor's, or a master's degree in the fields of applied sciences and/or arts, or a juris doctor degree. The university has received several large institutional grants to enhance the CaP research abilities of faculty, students, and its infrastructure as African

American men have a 60% higher incidence rate of CaP and twice the death rate of Caucasian men. CaP is also the second leading cause of cancer-related death in AA men. Paucity of investigators who conduct research on CaP disparities in minorities has often been cited as one of the barriers to research addressing minority health issues. UDC has established a strong partnership with the Lombardi Comprehensive Cancer Center (LCCC) at Georgetown University (GU) in Washington, DC. Historically, GU has a long-standing commitment to the recruitment and successful placement of minority trainees. The tumor Biology program - under the leadership of Deepak Kumar, PhD, Chair of Department of Biology at UDC - has been very successful at recruiting and retaining these individuals in their training program. In the past three years, Dr. Kumar has also built tremendous collaborations with USU-CPDR toward the summer training of UDC students in CaP research.

Uniformed Services University of the Health Sciences (USU) has a worldwide reputation as a center of excellence for military and public health professionals in their education and research. USU



programs are unique, related directly to enforce health protection, tropical diseases, disaster medicine, military and public health medical readiness, and adaptation to extreme environments. USU prepares outstanding scientists and health care practitioners for careers in service to the nation (www.usuhs.mil). USU-CPDR has been recognized by the DoD as the

Integrated Translational Prostate Disease Research Center of Excellence with an outstanding track record for more than 20 years. CPDR integrates state-of-the-art basic and clinical science research programs and an infrastructure supporting long-term biospecimen banks, a multicenter CaP patient database and training programs for post-doctoral fellows, urology residents, and students (USUHS medical and graduate students and college and high school interns). USUHS-CPDR program affiliations include Walter Reed Army Medical Center (WRAMC) and the Joint Pathology Center (JPC), formerly known as Armed Forces Institute of Pathology (AFIP).

The objectives of the HBCU training award were:

- To recruit and motivate highly qualified undergraduate trainees from UDC
- To provide them with a stimulating and intellectual environment that promotes state-of-the art training and education in CaP research
- To motivate young researchers who may contribute to CaP research at Historically Black Colleges and Universities (HBCUs)

Each student admitted to the program was assigned to one of the faculty members affiliated with CPDR who served as research mentor. Students carried out a specific research project that was designed to yield some exciting data and findings within the 12-week period. Through regular laboratory meetings, seminars, and personal discussions, the students interacted with other fellow students, faculty members, and staff. At the end of the summer experience, students presented their research findings and submitted their progress reports. Each student was given a certificate of completion of achievement. In the three years of this grant period, we have trained 16 UDC undergraduate students (four more than proposed in the grant) and it has been an extremely positive and enriching experience for both the faculty members and the students. Dr. Albert Dobi (2008) and Dr. Taduru Sreenath (2009-2010), Assistant Directors of the CPDR provided outstanding educational program directions under the general guidance of Dr. Shiv Srivastava (USU) and Dr. Deepak Kumar (UDC).

BODY:

Task 1.

Selection Process: USU/CPDR summer internship program announcements for 2008, 2009 and 2010 were made by Dr. Deepak Kumar (Partnering PI) at the UDC, encouraging application from undergraduate students, interested in pursuing an advanced education in medicine or medical research (Attachment 1-3). The completed applications considered for the selection process consisted of an essay describing the student's interest, academic transcripts, and letters of recommendation. In the three years of the grant period, sixteen students whose grade point average ranged from 3.2 to 3.8 were selected. The selection committee, consisted of the UDC and USU faculty advisors, the principal investigator (PI), and the Co-PI. Students were selected based on their academic credentials and interest in research.

2008:

Mr. Chiedozie Joseph Ayika

Mr. Francisco Saenz

Mr. Emmanuel Woode

Ms. Fiteh Yelekal

2009:

Ms. Zainab Afzal

Ms. Emelia Daka

Ms. Heran Kalyie

Mr. Benjamin Ozokwere

Mr. Henoke Shibeshi

Ms. Tseday Tegegn

Ms. Preety Upadhyay

2010:

Ms. Nicola Eva Abdul

Ms. Zainab Afzal

Ms. Juliet Chijioke

Ms. Christelle Donfack

Mr. Habib Kedir

Research Environment:

CPDR (www.cpdr.org) is committed to a multi-disciplinary approach to CaP research with over 350



publications and continues to make great strides in clinical and basic science research for improving the entire spectrum of care to include diagnosis, treatment, management, and follow-up for prostate cancer patients. The Center's strategy is to focus investigators on potential breakthrough research within its three major research programs (Basic Science, Clinical Science, and Patient Database) while maintaining the core support requirements for all of its programs. CPDR research focuses on discovery or validation of biologically

significant molecular defects in CaP onset or progression towards developing novel strategies in molecular classification and treatment of the CaP. Recent ground-breaking basic science and translational

investigations of the *ERG* as one of the most common oncogenic activations in CaP are among notable CPDR accomplishments. The CPDR program has also been in the lead on research focusing on CaP in African Americans, who are at highest risk of this disease. **The different components of the USU-CPDR and collaborations that have enriched the CaP research training of the UDC students included:**

- CPDR Basic Science Research Program (BSRP): This multi-disciplinary CaP research endeavor represents integration of collaborative efforts of 30 plus researchers (six PIs). State-of-the-art cancer biology laboratories at the Rockville, MD site and on USU campus in Bethesda support CaP biology and genetics focused research credited with discovery, functional and translational evaluations of prostate cancer-gene alterations with potential as biomarkers and therapeutic targets and development of strategies and resources for translational research.
- CPDR Prostate Cancer Clinical Center at WRAMC: The goals of the these efforts are to combine prostate screening, development and maintenance of long term bio-specimen banks, education and counseling, and prostate disease clinical trial research in an efficient, personal, patient-oriented center. This unique approach to the CaP clinical research has resulted in significant breakthroughs in these areas.
- USU-CPDR Multicenter National Database: CPDR has developed a comprehensive database of CaP patients with longitudinal follow-up within the DoD equal access health care context. With over 25,000 men enrolled to date the CPDR database has become a national resource that enables researchers to conduct important studies using existing data, preserving valuable time and resources.
- USU and AFIP Faculty: AFIP-Genitourinary Pathology Department faculty and staff who have collaborated with CPDR since its inception actively participated in training of UDC students. USU faculty with CaP research focus from Department of Anatomy, Physiology and Genetics and Department of Microbiology and Immunology actively participated in training of UDC students under the DoD-PCRP HBCU training program.

Multi-disciplinary team of cancer biologists, urologists, genitourinary pathologists, epidemiologists, biostatisticians, medical/bio-informatics and regulatory affairs specialists focuses on the following research areas:

- Discovery of frequent and potentially causal prostate cancer gene alterations
- Identification of biomarkers that will distinguish between indolent and aggressive CaP
- Development of new molecular strategies for improving prostate cancer diagnosis and prognosis
- Delineation of hormonal mechanisms involved in prostate cancer onset or progression
- Development and evaluation of novel molecular therapeutic agents for prostate cancer
- Development and maintenance of molecular specimen resources for translational research
- Development of new experimental models with focus on common prostate cancer gene alterations
- Identification of molecular determinants of prostate cancer susceptibility in high-risk groups such as African-Americans
- Epidemiologic research focusing on prognostic markers, racial disparity, obesity, outcomes of various modalities in CaP and quality of life of patients in relation to various treatments.
- Education of next generation of scientists in prostate cancer translational research

Task 2.

Assignment of Mentors and Projects: Students were assigned to the mentors and were provided with structured and realistic research projects. Students were exposed to a rich environment of knowledge bank, expert guidance, and tools to successfully complete the assignments. The knowledge and the technical experience they gained by engaging in experiments, seminars, discussions with scientists, and data presentations during the training period enhanced their understanding of CaP research and motivated them to pursue careers in basic science or clinical CaP research.

Mr. Chiedozie Joseph Ayika (2008)

Mentor: Meera Srivastava, PhD

Project title: Lack of p53 tumor suppressor effect in LNCaP cells is associated with FOXO3a

hyperphosphorylation.

Mr. Francisco Saenz (2008)

Mentor: Albert Dobi, PhD

Project title: Defining the role of NKX3.1 on the expression of *TMPRSS2-ERG* fusion gene.

Mr. Emmanuel Woode (2008)

Mentor: Gyorgy Petrovics, PhD

Project title: Biological function of truncated ERG protein.

Ms. Fiteh Yelekal (2008)

Mentor: Bungo Furusato, MD

Project title: Increased levels of SPARC (osteonectin) in human prostate cancer tissues and its association

with clinical metastasis.

Ms. Zainab Afzal (2009)

Mentor: Shyh-Han Tan, PhD

Project title: ERG is a transcription factor which belongs to the ETS family.

Ms. Emelia Daka (2009)

Mentor: Albert Dobi, PhD

Project title: Defining mir-127 in benign epithelial cells of tumor bearing prostate glands.

Ms. Heran Kalyie (2009)

Mentor: Johnan Kaleeba, PhD

Project title: Human Herpes Virus 8 in prostate cancer initiation and progression.

Mr. Benzamin Ozokwere (2009)

Mentor: Taduru Sreenath, PhD

Project title: Functional analysis of ERG: Role in trans-differentiation.

Mr. Henoke Shibeshi (2009)

Mentor: Meera Srivastava, PhD

Project title: Tumor suppressor activity of Annexin A7 in prostate cancer.

Ms. Tseday Tegegn (2009)

Mentor: Gyorgy Petrovics, PhD

Project title: Functional analysis of ERG in prostate cancer cells

Ms. Preety Upadhyay (2009)

Mentor: Dr. Albert Dobi, PhD

Project title: Assessing *ERG* as a regulator of ARR2-Probasin promoter.

Ms. Nicola Eva Abdul (2010)

Mentor: Taduru Sreenath, PhD

Project title: TMPRSS2-ETS related gene fusions in mouse models for prostate cancer.

Ms. Zainab Afzal (2010)

Mentor: Jane Hudak, RN, PhD

Project title: CPDR Multi-disciplinary Prostate Cancer Clinic: Educational experience shadowing patients

diagnosed with prostate cancer.

Ms. Christelle Donfack (2010)

Mentor: Ahmed Mohamed, MD, PhD

Project title: Characterization of ERG protein in prostate cancer and other tumor cell lines.

Ms. Juliet Chijioke (2010)

Mentor: Hua Li, MD, PhD

Project title: Androgen receptor regulates NEDD4-1, an oncogenic protein, in prostate cancer cells.

Mr. Habib Kedir (2010)

Mentor: Gyorgy Petrivics, PhD

Project title: Urine based prostate cancer diagnostic assay development.

Task 3.

Training, **Goals**, **and Objectives:** Each student carried out the research assignment with a specific objective that was designated to yield some new data and findings within the 12-week period.

Provided below is students' impression of their project goals with minor edits:

Mr. Chiedozie Joseph Ayika (2008)

Apoptosis detection assays and cell cycling showed that p53 failed to match programmed cell death (PCD), and cell growth arrest that were induced by ANXA7 in androgen-responsive prostate cancer cells

(LNCaP). The main objective was to examine whether p53 and ANXA7 pathways control cell proliferation and determine whether they work independently or in the same pathway.

Mr. Francisco Saenz (2008)

A cure for cancer can only start with better diagnosis and the molecular mechanisms underlying the disease and later development of new and better treatment. Hence, the objective was to define the role of NKX3.1 on the expression of *TMPRSS2-ERG* fusion gene. The results would represent a step further towards the understanding of molecular mechanisms of prostate tumorigenesis.

Mr. Emmanuel Woode (2008)

Three of the five ERG isoforms were identified at CPDR as full length prototypical gene product (type I) while the remaining two were identified to be truncated and without the ETS binding domain (type II). We hypothesize that the truncated forms act as dominant negative. Thus the truncated variants may suppress the function of the full length type.

Ms. Fiteh Yelekal (2008)

Comparative gene expression signatures of well/moderately differentiated and poorly differentiated prostate cancer (CaP) cells and transcriptional regulation analyses highlighted alterations of *SPARC*, and genes linked to it, in poorly differentiated CaP. Our objective is to study SPARC protein expression in a large cohort of patients by immunohistochemistry, whether the protein expression of SPARC can predict aggressive clinical behavior in retrospectively selected cohort of patients.

Ms. Zainab Afzal (2009)

ERG oncogene is activated in two-thirds of CaP patients. CPDR researchers defined qualitative and quantitative features of two main types of ERG transcripts in CaP. The goals of the project was to study the sub-cellular localization of the different isoforms of Type I: ERG: ERG1, ERG2, WT-ERG3, TM-ERG3, and Type II ERG: TM-ERG8 and to determine their transcriptional activity.

Ms. Emelia Daka (2009)

The function of miRNAs is largely unexplored in CaP. The objective of this study was to define how mir-21 and mir-127 regulate ERG that is expressed in the majority of CaP patients.

Ms. Heran Kalyie (2009)

To determine the mechanism by which Kaposi Sarcoma Herpes Virus (KSHV) may skew the endogenous cellular processes toward a state that results in aggressive growth of CaP cells.

Mr. Benjamin Ozokwere (2009)

CaP cells are known to metastasize to bone as the cancer progresses to hormone independence or refractory stage. The objective of this project was to determine whether ERG influences transdifferentiation of CaP cells into bone cells.

Mr. Henoke Shibeshi (2009)

The objective of this study was to examine if the tumor suppression activity of ANXA7 involves FGF8 in CaP cell lines (LNCaP, DU145, and PC3) and their normal counterpart (PrEC).

Ms. Tseday Tegegn (2009)

To study the role of ERG in regulating the expression of other genes using cell-line models. The other objective was to explore whether patients with ERG overexpression in their prostate tumor may have a lower serum prostate-specific antigen (PSA) level compared to patients with ERG-negative prostate tumors.

Ms. Preety Upadhyay (2009)

To assess a new aspect of ERG transcription-factor function by studying its regulation of probasin promoter (*ARR2PB*) commonly used in the generation of CaP transgenic mouse models. Two independent approaches were applied: (1) bioinformatic definition of ETS-binding sites in *ARR2PB* promoter sequence, and (2) assessment of *ERG* as repressor or activator for the probasin promoter in CaP cells.

Ms. Nicola Eva Abdul (2010)

Gene rearrangements leading to The TMPRSS2- Ets related gene (ERG) fusions in prostate cancer are of extreme importance, due to their high prevalence among prostate cancer patients. The cause of the gene fusions alone is not clearly understood yet. In this study, we planned to examine if proteins from biological factors such as SV40 virus caused rearrangements in mouse models.

Ms. Zainab Afzal (2010)

Shadowing a number of patients during various stages of prostate cancer diagnosis, treatment and recovery, as well as being mentored by many clinical staff members will provide a rich educational opportunity to understand this disease from the clinician's and the patient's perspective.

Ms. Christelle Donfack (2010)

Our objective was to understand the oncogenic functions of ERG by examining the localization, the expression size and quantity of ERG in prostate and other tumor cell lines such as Colo320, Molt4, KG-1, and VCaP by Western blot analysis and Immunofluorescence analysis.

Ms. Juliet Chijioke (2010)

The androgen receptor (AR) plays an essential role in the differentiation and growth of the prostate gland. The stability of androgen receptor depends on MDM2-p53 stress response pathway and PMEPA1-NEDD4-1 feedback loop, to maintain its overall homeostasis. However, the combined mechanism of PMEPA1 and NEDD4-1 to degrade AR is still not clear. Our objective was to study cooperativity of PMEPA1 and NEDD4 in degradation of AR signaling in prostate cancer.

Mr. Habib Kedir (2010)

Our objective was to develop a noninvasive urine based prostate cancer diagnostic assay with better sensitivity and specificity. Experiments focused on the stability and recovery prostate cancer cells spiked into urine using a variety of fixatives and recovery platforms.

Task 4.

Scheduled meetings/activities to monitor student's progress.

Student and mentors met every morning to discuss the plan for the experiments and in the evenings to summarize the experimental results and interpretations. Students also attended the following meetings:

- Weekly meetings: Students participated in department seminars presented by USU/CPDR faculty and
 researchers, as well as guest speakers, to understand the research activities and the progress in the field
 of CaP.
- **Biweekly seminar presentations:** Students presented their goals, objectives, and experimental plan for the training period in the first presentation and their progress in subsequent presentation.
- At the end of the summer experience, each student prepared and presented their research findings as PowerPoint presentations.
- Final seminar presentation: Students presented the complete project report and conclusions.
- **Report Submission:** Each student submitted the entire project as a hard copy and an electronic version to the supervisors.

 $\begin{tabular}{ll} Table 1. Programmed interaction and oversight of the student interns by the PI and Co-PI, faculty advisors, and mentors \\ \end{tabular}$

TimeLine	Process	Action	Responsibility
l 2 weeks prior to Internship start date	App lications	Selection	CPDR-USU and UDC Selection committee
8 weeks prior to Internship start date	Mentors for the program	Appointment	Program Director (PD) and Co-Pis
4 weeks prior to Internship start date	Research Projects	Goals and Objectives	Mentors
2 weeks prior to Internship start date	Research Projects	Approvals	Program Director (PD) and Co-Pls
Day 1	Internship start date	Lab Orientation	Mentors and Students
Week 1	Student Research Goals and Objectives	Weekly Review	Meniors and Students
Week2	Student Research Progress	Bi-Weekly Review and Presentations	PD, Co-PIs, Mentors and Students
Week 4	Student Research Progress	1st Monthly Review	PD, Co-PIs, Faculty Advisors Mentors and Students
Week 8	Student Research Progress	2nd Monthly Review	PD, Co-PIs, Mentors and Students
Week 10	Student Research Progress	Semi-final Review	PD, Co-Pis, Mentors and Students
Week 11	Completion of Research Experiments	Review and Approval	PD, Co-PIs and Mentors
Week 12	Submission of Research Report	Final Presentation	PD, Co-PIs, Faculty Advisors Mentors and Students

KEY RESEARCH ACCOMPLISHMENTS OF SUMMER INTERNS:

All sixteen UDC students, selected under HBCU Summer Undergraduate Training Program in CaP Research, have successfully completed their projects assigned to them. Highlights of their project outline and experimental results are described below:

Mr. Chiedozie Joseph Ayika (2008)

Lack of p53 tumor suppressor effect in LNCaP cells is associated with FOXO3a hyper-phosphorylation.

- Lack of tumor suppressor effects of p53 in LNCaP prostate cancer cells was compared with ANXA7, which exhibited tumor suppressor activity. p53 significantly increased the phosphorylation of FOXO3A without any alteration in total FOXO3A protein
- Phosphorylated FOXO3A protein was predominantly localized to the cytoplasm in
- LNCaP cells infected with Adenovirus p53 vector.
- In contrast, ANXA7 did not affect either total or phospho- FOXO3A expression.

Conclusion: This is an intriguing finding, where ectopic p53 expression in LNCaP cells resulted in hyper-phosphorylation of FOXO3A and translocation to cytoplasm leading to its ubiquitination and subsequent degradation. Lack of nuclear FOXO3A may lead to a failure in inducing pro-apoptotic signals in LNCaP cells. This data may be specific to a given LNCaP variant used in this project, future studies are needed to further address this issue.

Mr. Francisco Saenz:

Defining the role of NKX3.1 on the expression of TMPRSS2-ERG fusion gene

- NKX3.1 and ERG are common gene defects in prostate cancer. Potential functional interactions between NK3.1 and ERG were evaluated. Comparative promoter and enhancer analysis of human, mouse and rat *TMPRSS2* promoters and promoter upstream sequences revealed high conservation of the positions and frequency of NKX3.1 binding sites
- Inhibition of NKX3.1 by siRNA treatment resulted in elevated expression of ERG in VCaP cells, indicating the activation of *TMPRSS2-ERG* fusion gene
- NKX3.1siRNA treated VCaP cells have shown reduced levels of NKX3.1, higher levels of PSA and ERG protein by immune-florescence analysis

Conclusion: These results suggest that NKX3.1 negatively regulates the *TMPRSS2* promoter activity through binding to the conserved sites. The loss of its expression due to either decreased stability or monoallelic loss may result into elevated expression of ERG in the *TMPRSS2-ERG* fusion context of prostate cancer. These data suggest that two common gene defects in prostate cancer may work together to promote cancer and this information may lead to new ideas for treatment. This is a very important finding and is being actively pursued at CPDR.

Mr. Emmanuel Woode (2008)

Biological function of truncated ERG (ERG 8) protein

- ERG is a common oncogenic alteration in prostate cancer. Two types of ERG proteins: Type I, near full length isoforms (ERG 1, 2 and 3) and Type II, ETS domain lacking isoforms (ERG 8, EPC) are expressed in prostate cancer cells. While expression or function of ERG Type I isoforms are better understood in prostate cancer, more needs to be learned about ERG Type II isoforms.
- ERG3 (Type I isoform) and ERG 8 (type II isoform) expression vectors were used to successfully detect ERG 3 and ERG 8 proteins in HEK 293 cells experimental model.
- Si RNA specific to ERG 8 inhibited ERG8 but did inhibit ERG 3 expression in HEK293 cells and Si RNA specific to ERG 3 inhibited ERG 3 expression but did not inhibit ERG 8.

Conclusion: These results established first reagents necessary for further study of biological functions of ERG 8 in prostate cancer cells.

Ms.Fiteh Yelekal (2008)

Increased levels of *SPARC* (osteonectin) in human prostate cancer tissues and its association with clinical metastasis.

- Previous research at CPDR identified SPARC protein as a central node in the gene networks differentially expressed in poorly differentiated aggressive prostate cancers in comparison to moderate well differentiated tumors.
- High SPARC expression in CaP mRNA levels was associated with an increased risk of PSA recurrence.
- Comparative quantitative determination of SPARC protein by immuno-histochemistry showed significant association of high SPARC protein levels in primary tumor of patients with metastasis in comparison to primary tumors of patients without metastasis.

Conclusion: This study provided very promising results with respect to an early prognostic biomarker for prostate cancer progression which is being pursued actively by CPDR investigators.

Ms. Zainab Afzal (2009)

ERG is a transcription factor which belongs to the ETS family

- ERG is one of the most common oncogeneic activation known in prostate cancer. Different versions of ERG mRNA and proteins: Type I, near full length isoforms (ERG 1, 2 and 3) and Type I1, ETS domain lacking isoforms (ERG 8, EPC) are expressed in prostate cancer cells. Using HEK293 cell culture model and ectopic expression of various ERG forms, their subcellular localization and transcription factor function were studied. The Type I ERG isoforms, ERG1, ERG2, WT-ERG3, and TMPRSS2-ERG3 were localized to the nucleus.
- The type II ERG,TMPRSS2-ERG8 was localized to the cytoplasm.

• Type I ERG isoforms showed strong ERG transcription activity where as type II ERG isoform was virtually inactive.

Conclusion: These results suggested that ETS DNA-binding domain is required for the nuclear localization of a ERG protein. Transcriptional efficacy of ERG isoforms using reporter assays revealed that the nuclear localization of ERG isoforms is required for their function as trancription regulators. It remains to be established if there is any interaction between Type I and Type II ERG proteins which is currently being studied at CPDR.

Ms. Emelia Daka (2009)

Defining mir-127 in benign epithelial cells of tumor bearing prostate glands

- ERG is one of the most common oncogeneic activation known in prostate cancer. Potential regulation of ERG expression by micro-RNAs was studied. Micro-RNA sites were identified in ERG sequence by bio-informatics analyses. ERG 3' UTR sequence contained mir-127 and mir-21 binding sites.
- mir-127 was present in benign prostate tissue away from prostates tumors.
- mir-127 was undetected in ERG expressing prostate cells

Conclusion: Presence of mir-127 expression in benign prostate cells and lack of its expression in tumor cells suggested a potential negative regulatory function of mir-1271 in controlling ERG expression. These novel findings deserve further study.

Ms. Heran Kalyie (2009)

Human Herpes Virus 8 in prostate cancer initiation and progression

- Role of pathogens in prostate cancer onset remains a hot topic, however, there is no firm data to support biological role of viruses or bacteria in prostate cancer. This study focused on the assessment of HHV8, which is associated with Kaposi Sarcoma, in prostate cancer cell lines. CaP cell lines can be infected with a KSHV based on virion entry using KSHV219.
- In cell invasion, KSHV infected CaP cells (DU-145) had the tendency to invade faster compared to uninfected DU-145
- KSHV infection may stimulate the growth of prostate tissue, leading to a more aggressive disease

Conclusion: The results suggested that KSHV may be present in prostate cancer cell lines including LNCaP, DU145 and PC3. Presence of KSHV in prostatic reservoir may lead to initiation and/or progression of prostate cancer. More work is warranted to confirm these intriguing results.

Mr. Benjamin Ozokwere (2009)

Functional analysis of ERG: Role in trans-differentiation

- Since ERG is the most common cancer gene defect in prostate cancer and prostate cancer is known to metastasize to bone, potential role of ERG in bone metastasis was studied. VCaP cells (derived from a human vertebral metastatic lesion of CaP) expressing high levels of ERG trans-differentiates into osteogenic cells in the presence of osteogenic media conditions.
- Down regulation of ERG expression was achieved using ERG siRNA.
- Downregulation of ERG in VCaP cells blocks the osteogenic potential of VCaP cells in the presence of osteogenic media conditions

Conclusion: ERG knockdown experiments showed new insights in that ERG influences the increased calcium accumulation in VCaP cells indicating its potential role in regulating osteogenesis. Further studies will address potential role of ERG in bone metastasis.

Mr. Henoke Shibeshi (2009)

Tumor suppressor activity of Annexin A7 (ANXA7) in prostate cancer

- ANXA7 functions as a tumor suppressor gene in animal model and human prostate cancer cell culture models. Effects of wt ANX7 and its dominant negative mutant were analyzed on FGF8 expression in prostate epithelial cells.
- In PrEC cells, expression of FGF8 was negatively regulated by adenovirus vector expressing full-length ANXA7 but not by adenovirus vector expressing DN-ANXA7 or control adenovirus vector.
- Expression of WT ANXA7 in PrEC cells inhibited cell growth.

Conclusion: WT-ANXA7 inhibits FGF8 expression which may contribute to inhibition of prostate epithelial cell proliferation. Loss of ANX7 in prostate tumors may contribute to prostate cancer cell proliferation.

Ms. Tseday Tegegn (2009)

Functional analysis of ERG in prostate cancer cells

- ERG is a potentially causal common oncogenic alteration in prostate cancer. Cancer biologic properties of ERG were analyzed by ERG silencing in a prostate cancer cell line (VCaP) and by overexpression of ERG in an immortalized normal prostate cell line (BPH1). ERG knockdown inhibited the cell growth and altered the morphology of VCaP cells. ERG knockdown in VCaP cells correlated with increased PSA and other prostate differentiation markers.
- ERG overexpression in BPH1 cells showed an increased cell migration as compared to the control BPH1 cells.
- Reciprocal relationship of ERG and PSA was further analyzed in prostate cancer patients. Data analysis shows that patients with \(\leq 4ng/mL \) serum PSA had higher frequency of ERG positive CaP (ERG

positive, 79% vs. ERG negative, 67%) than patients with > 4 ng/mL serum PSA (ERG positive, 56% vs. ERG negative, 52%)

Conclusion: ERG knockdown experiments in VCaP cells and overexpression studies in BPH1 cell lines highlighted pro-cancer functions of ERG.

Ms. Preety Upadhyay (2009)

Assessing ERG as a regulator of ARR2-Probasin promoter

- Previous studies from CPDR suggested that ERG may inhibit androgen receptor (AR) functions.
 ARR2-probasin promoter is AR regulated and has been commonly used in the generation of prostate
 targeted transgenic mouse. Due to difficulties in generating ARR2-probasin promoter driven ERG
 transgenic mice in several laboratories, there has been concern over less optimal function of ARR2 probasin promoter, likely due to inhibition of AR by ERG. Using transcriptional trans-activation assay,
 effect of ERG was evaluated on ARR2-probasin promoter.
- Transcriptional activation assays indicate that ERG acts as a repressor of *ARR2PB*-driven luciferase gene in LNCaP cells.
- No significant change in ARR2PB-Luc activity in VCaP with ERG

Conclusion: ERG suppresses the ARR2PB promoter. The lack of suppression of transcriptional activity in VCaP cells may be explained as VCaP cells express high levels of endogenous ERG. These data suggested for evaluation of potential effects of ERG on ARR2-PB promoter in mouse prostate cells.

Ms. Nicola Eva Abdul (2010)

TMPRSS2-ETS related gene fusions in mouse models for prostate cancer

- *TMPRSS2-ERG* gene fusions are common in human prostate cancer. Using Erg protein expression as a surrogate for the *Tmprss2-Erg* alterations, prostate tumors from the TRAMP transgenic mouse were assessed for gene fusions.
- Wild type mice showed Erg expression only in endothelial cells of prostate. ERG transgenic mice showed abundant ERG protein expression in the nucleus of prostate luminal epithelial cells, in addition to endogenous Erg expression in endothelial cells.
- TRAMP mouse prostates showed expression mostly in the endothelial cells
- Focal ERG expression was seen in the luminal epithelial cells of only 1 out of 50 TRAMP mouse prostates.

Conclusion: The factors that induce specific chromosomal rearangements of *TMPRSS2-ERG* are not well defined. Although, biological factors such as viruses are suspected to be causative factors, specific chromosomal rearrangements in prostate cancer have not been characterized. **Our experiments using TRAMP mouse prostates did not show a convincing evidence of ERG alterations in TRAMP mice**.

Ms. Zainab Afzal (2010)

CPDR Multi-disciplinary Prostate Cancer Clinic: Educational experience shadowing patients diagnosed with prostate cancer

- CPDR Multi-disciplinary clinic is a state-of-the-art treatment facility at the Walter Reed Army Medical
 Center for patients undergoing treatment for prostate cancer. It is also a great learning environment for
 residents and medical students. This nursing student during her second term at CPDR requested for the
 internship opportunity at the clinic. Under the guidance of a nurse educator, she interacted with
 prostate cancer patients through various stages of diagnosis, treatment options and recovery.
- She developed a great perspective on how differently each patient reacted and coped to the diagnosis of prostate cancer.
- She also developed a better understanding of various treatments being offered to patients.
- She related her experience to fellow students doing cancer biology research in the laboratory.

Conclusion: Shadowing a number of patients during various stages of prostate cancer diagnosis, treatment and recovery, as well as being mentored by many clinical staff members, afforded a rich educational opportunity to understand this disease from the clinician's and the patient's perspective.

Student: Ms. Christelle Donfack (2010)

Characterization of ERG protein in prostate cancer and other tumor cell lines

- Although ERG gene was discovered almost 24 years ago, good quality ERG specific antibodies were
 not available for confident evaluation of ERG protein in experimental models and human cancers.
 Recent development of highly specific ERG monoclonal antibody at CPDR has led to first
 opportunities in the evaluation of ERG protein in diverse cancer research contexts. To understand ERG
 protein functions in different cancer types and normal context, ERG protein expression was analyzed in
 HUVEC (normal endothelial cells), COLO 320 (colon carcinoma), NCI-H660 (prostate carcinoma),
 VCaP (prostate carcinoma), KG1 (acute myelogenous leukemia) and MOLT4 (acute lymphoblastic
 leukemia) cell lines.
- ERG siRNA effectively downregulated ERG expression in HUVEC, COLO 320, NCI-H660 and VCaP cells. This also established the specificity of ERG MAb for ERG protein detection in different tumor cell lines.
- ERG protein was predominantly detected in the nucleus of endothelial cells and prostate cancer and leukemia cell lines. ERG protein was detected in nucleus as well as cytoplasm of colon cancer cell line.

Conclusion: ERG is a nuclear transcription factor and regulates the expression of downstream target genes. Although, ERG protein is seen in various tumors and HUVEC cells, the molecular weights and levels of expression were varied. ERG protein was localized in the nucleus of KG1, MOLT4, COLO320 and VCaP. In addition to nucleus, COLO320 cells also showed ERG expression in cytoplasm. These data laid the foundation for evaluation of ERG function cell lines from different cancers which could lead to optimal therapeutic strategies.

Ms. Juliet Chijioke (2010)

Androgen receptor (AR) regulates NEDD4-1, an oncogenic protein, in prostate cancer cells.

- AR plays important role in normal prostate development and differentiation. Previous research at CPDR established a new mechanism of regulation of the AR by an androgen regulated protein, PMEPA1, which binds to NEDD4. In continuation of these studies effects of AR on NEDD4-1 was evaluated. AR was up-regulated by synthetic androgen R1881 in both LNCaP and VCaP cells.
- The over-expression of wild-type and T877A mutated AR via adenovirus expression vectors induced the expression of NEDD4-1 in LNCaP cells
- Knockdown of androgen receptor led to down-regulation of NEDD4-1 in LNCaP cells. Furthermore, knockdown of PMEPA1 in LNCaP cells that upregulates AR, induced expression of NEDD4-1 in androgen dependent manner

Conclusion: Loss of *PMEPA1* expression results in the elevation of androgen receptor levels and androgen signaling. NEDD4-1 is an oncoprotein and its expression is androgen inducible. Loss of *PMEPA1* may lead to the activation of NEDD4-1 proto-oncoprotein. These data suggested that loss or reduced expression of PMEPA1 in prostate cancer cells increases AR levels, which in turn may activate pro-cancer protein such as NEDD4. **These findings provide new insights into role of AR protein regulation and its downstream effects in prostate cancer.**

Mr. Habib Kedir (2010)

Urine based prostate cancer diagnostic assay development

- Due to continued interest in the development of minimally invasive urine based diagnostic assays at CPDR, new assay platforms are being tested for the stability and recovery of prostate cancer cells spiked into urine. Different fixatives were tested.
- Morphology and quantification of prostate cancer cells recovered from urine has led to development of an optimized protocol.
- Recovered cells could be evaluated by nuclear staining

Conclusion: A more sensitive and reproducible method of cell recovery from urine was achieved. Further development of assays for downstream applications is needed.

REPORTABLE OUTCOMES:

During the internship, students displayed tremendous interest in the field of CaP. They were highly motivated in learning and doing experiments, as well as in educating themselves on important issues in prostate cancer research and treatment. The results obtained from their experiments were presented as posters in HBCU conferences at the national level and were awarded scientific merit awards.

- At the end of the training period oral presentations were made by students in the presence of faculty and staff of the CPDR and senior leaderships of the USU (Department Chairman) and UDC (Dean, College of Arts and Sciences). Selected poster presentations were made by students at the USUHS Research Week (2010, 2011) and UDC Undergraduate Research Day (2009, 2010).
- Selected oral presentations and poster presentations were made by students at the HBCU-UP National Research Conferences (Atlanta, GA, 2008; Washington, D C, 2009) and Annual Meetings of the BKX/NIS (Norfolk, VA, 2009; New Orleans, LA, 2010; Atlanta, GA 2011).

Meeting Presentations:

HBCU-UP National Research Conference, Atlanta, GA (2008)

Francisco Sáenz, Rajesh Thangapazham, Deepak Kumar, Shiv Srivastava, and Albert Dobi. A Role for Conserved Regulatory Sequences in the Repression of TMPRSS2-ERG Fusion Gene, a Prevalent Oncogenic Alteration in Prostate Cancer. HBCU-UP National Research Conference, Atlanta, Georgia.

Emmanuel Woode, Ying Hu, Gyorgy Petrovics, Deepak Kumar, and Shiv Srivastava. Evaluation of the Variants of ERG Oncogene in Prostate Cancer. HBCU-UP National Research Conference, Atlanta, Georgia.

Chiedozie J. Ayika, Katerina Mezhevaya, Meera Srivastava, Yelizaveta Torosyan,, Deepak Kumar, and Shiv Srivastava. The Lack of p53 Tumor Suppressor Effects in LNCaP was Associated with FOXO3a Hyperphosphorylation. HBCU-UP National Research Conference, Atlanta, Georgia.

Yelekal Fitch, Deepak Kumar, Y. Fitch, B. Furusato, C.A. DeRosa, Y. Chen, L. Ravindranath, C. Cook, J. Cullen, D.G. McLeod, G. Petrovics, I.A. and Sesterhenn, S Srivastava. Osteonectin (SPARC) Expression Correlates with PSA Recurrence after Radical Prostatectomy. HBCU-UP National Research Conference, Atlanta, Georgia.

66th Annual Meeting of the BKX/NIS, Norfolk, VA (2009)

Yelekal Fiteh, Deepak Kumar, Y. Fiteh, B. Furusato, C.A. DeRosa, Y. Chen, L. Ravindranath, C. Cook, J. Cullen, D.G. McLeod, G. Petrovics, I.A. and Sesterhenn, S Srivastava. Osteonectin (SPARC) Expression Correlates with PSA Recurrence after Radical Prostatectomy.

UDC Undergraduate Research Day Washington DC (2009)

Yelekal Fitch, Deepak Kumar, Y. Fitch, B. Furusato, C.A. DeRosa, Y. Chen, L. Ravindranath, C. Cook, J. Cullen, D.G. McLeod, G. Petrovics, I.A. and Sesterhenn, S. Srivastava. Osteonectin (SPARC) Expression Correlates with PSA Recurrence after Radical Prostatectomy.

Emmanuel Woode, Ying Hu, Gyorgy Petrovics, Deepak Kumar, and Shiv Srivastava. Evaluation of the Variants of ERG Oncogene in Prostate Cancer.

HBCU-UP National Research Conference Washington DC (2009)

Benjamin Ozokwere, Ahmed Mohamed, Deepak Kumar, Shiv Srivastava and Taduru Sreenath Functional Analysis of ERG: Role in Trans-differentiation.

Henoke D Shibeshi, Ximena Leighton, Yelizaveta Torosyan, Deepak Kumar, Shiv Srivastava and Meera Srivastava. Distinct Tumor Suppressor Effects of WT- versus DN-Annexin A7 (ANXA7) Involve Fibroblast Growth Factor (FGF8).

Heran Kalyie, Deepak Kumar, Shiv Srivastava and Johnan Kaleeba. Human Herpes Virus 8 in Prostate Cancer Initiation and Progression.

Zainab Afzal, Deepak Kumar, Shiv Srivastava and Shyh-Han Tan. Subcellular Localization and Transcriptional Activity of ERG Isoforms.

Preety Upadhyay, Deepak Kumar, Shiv Srivastava and Albert Dobi. *ERG* is a Transcriptional Repressor of Probasin Promoter (*ARR2PB*).

Emelia Daka, Deepak Kumar, Shiv Srivastava and Albert Dobi. Defining mir-127 in Benign Epithelial Cells of Tumor Bearing Prostate Glands.

Tseday Tegegn, Lakshmi Ravindranath, Deepak Kumar, Shiv Srivastava and Gyorgy Petrovics. Functional Analysis of ERG in Prostate Cancer Cells.

67th Joint Annual Meeting of NIS/BKX, New Orleans, LA (2010)

Benjamin Ozokwere, ETS Related Gene (ERG) Regulates Osteogenesis.

Zainab Afzal, Subcellular Localization and Transcriptional Activity of ERG Isoforms.

Fitch Yelekal, Voltage-Gated Sodium Channel Nav1.8 Expression in Human Prostate Carcinoma and Anti-Tumor Activity of Sodium Channel Blocker (R) Icm-I-136 in Human Prostate Carcinoma.

68thJoint Annual Meeting of NIS/BKX, Atlanta, GA. February (2011)

Nicola Eva Abdul, TMPRSS2- Ets Related Gene Fusions in Mouse Models for Prostate Cancer.

Juliet Chijioke, Androgen Receptor Regulates NEDD4-1, an Oncogenetic Protein, in Prostate Cancer Cells.

USU Research Day, Bethesda MD (2010)

Tseday Tegegn, Benjamin Ozokwere, Ahmed Mohamed, Deepak Kumar, Taduru Sreenath, Gyorgy Petrovics and Shiv Srivastava. Ets Related Gene Regulates the Cancer Phenotype in Prostate Epethelial Cells.

Zainab Afzal, Preethy Upadhyay, Emelia Daka, Shyh-Han Tan, Deepak Kumar, Taduru Sreenath, Albert Dobi, and Shiv Srivastava. Subcellular Localization and Transcriptional Activity of ERG Isoforms.

USU Research Day, Bethesda MD (2011)

Zainab Afzal, Tseday Zewdu Tegegn, Taduru Sreenath, Deepak Kumar, Shiv Srivastava² and ShyhHan Tan. Subcellular Localization and Transcriptional Activity of ERG Protein Encoded by the Common *TMPRSS2-ERG* Splice Variants Expressed in Prostate Cancer.

Francisco Sáenz, Rajesh Thangapazham, Deepak Kumar, Shiv Srivastava and Albert Dobi. A Role for Conserved Regulatory Sequences in the Repression of *TMPRSS2-ERG* Fusion Gene, a Prevalent Oncogenic Alteration in Prostate Cancer

Deepak Kumar, Taduru Sreenath, Albert Dobi, Gyorgy Petrovics, Bungo Furusato, Shy-Han Tan, Hua Li, Mohamed Ahmed, Rajesh Thangapazham, Ying Hu, Jane Hudak, Isabell A. Sesterhenn, Meera Srivastava, Johnan A.R. Kaleeba, David G. McLeod and Shiv Srivastava. HBCU Summer Undergraduate Training Program in Prostate Cancer Research: A partnership between the Uniformed Services University of the Health Sciences (USU)-Center for Prostate Disease Research (CPDR) and The University of the District of Columbia (UDC).

Innovative Minds in Prostate Cancer Today (IMPaCT) Conference, Orlando, FL (2011)

Zainab Afzal, Tseday Zewdu Tegegn, Taduru Sreenath, Deepak Kumar, Shiv Srivastava and Shyh-Han Tan. Subcellular Localization and Transcriptional Activity of ERG Protein Encoded by the Common *TMPRSS2-ERG* Splice Variants Expressed in Prostate Cancer.

Francisco Sáenz, Rajesh Thangapazham, Deepak Kumar, Shiv Srivastava and Albert Dobi. A Role for Conserved Regulatory Sequences in the Repression of *TMPRSS2-ERG* Fusion Gene, a Prevalent Oncogenic Alteration in Prostate Cancer.

Deepak Kumar, Taduru Sreenath, Albert Dobi, Gyorgy Petrovics, Bungo Furusato, Shy-Han Tan, Hua Li, Mohamed Ahmed, Rajesh Thangapazham, Ying Hu, Jane Hudak, Isabell A. Sesterhenn, Meera Srivastava, Johnan A.R. Kaleeba, David G. McLeod and Shiv Srivastava. HBCU Summer Undergraduate Training Program in Prostate Cancer Research: A partnership between the Uniformed Services University of the Health Sciences (USU)-Center for Prostate Disease Research (CPDR) and The University of the District of Columbia (UDC).

Awards received by students:

2008 Students

3rd Place- Biological Sciences (Oral presentation): **Francisco Sáenz**, A Role for Conserved Regulatory Sequences in the Repression of TMPRSS2- ERG Fusion Gene, a Prevalent Oncogenic Alteration in Prostate Cancer. HBCU-UP National Research Conference, Atlanta, GA (2008).

3rd Place- Biological Sciences (Poster presentation): **Emmanual Woode**, Evaluation of the Variants of ERG Oncogene in Prostate Cancer. UDC Undergraduate Research Day (2009).

3rd Place- Biological Sciences (Poster presentation): **Yelekal Fitch**, Osteonectin (SPARC) Expression Correlates with PSA Recurrence after Radical Prostatectomy. UDC Undergraduate Research Day- (2009)

2009 Students

1st Place- Biological Sciences (Oral Presentation): **Benjamin Ozokwere**, Functional Analysis of ERG: Role in Transdifferentiation. HBCU-UP National Research Conference. Washington, DC, (2009)

1st Place- Biology C (Oral Presentation): **Benjamin Ozokwere**, ETS Related Gene (Erg) Regulates Osteogenesis. 67th Joint Annual Meeting of NIS/BKX, New Orleans, LA. (2010). 1st Place- Biology (Oral Presentation): **Henoke Shibeshi**, The Effect Of Annexin A7 on The Expression of FGF8 In Prostate Cancer. University of the District of Columbia Undergraduate Research Day, (2010).

1st Place- Biology (Poster Presentation): **Emelia Daka**, Defining Mir-1271 in Benign Epithelial Cells of Tumor Bearing Prostate Glands. University of the District of Columbia Undergraduate Research Day, (2010).

2nd Place (Oral Presentation) Biology: **Heran H. Kalyie**, The Role of Kaposi Sarcoma-Associated Herpes Virus (Kshv) in Prostate Cancer. University of the District of Columbia Undergraduate Research Day, (2010).

2nd Place Biology A (Oral Presentation): **Zainab Afzal**, Subcellular Localization and Transcriptional Activity of ERG Isoforms. 67th Joint Annual Meeting of NIS/BKX, New Orleans, LA (2010).

2010 Students

2nd Place (Oral Presentation) Biology: **Nicola Abdul**, TMPRSS2- Ets Related Gene Fusions in MouseModels for Prostate Cancer, 68th Joint Annual Meeting of NIS/BKX, Atlanta, GA (2011).

3rd Place- Biological Sciences (Poster presentation): **Place Juliet Chijioki** Regulation of Androgen Receptor Levels through the PMEPA1-NEDD4-1 Feedback Loop. 68th Joint Annual Meeting of NIS/BKX, Atlanta, GA (2011).

Student expressions after completing the training:

"I'm standing in between either going ahead with my childhood dream of going to medical school or major into research. This has been an experience of a life time, which is the beginning of many more things to come." (Emelia Daka)

"My dad was diagnosed with prostate disease about a year ago. I understand the importance of the prostate diseases research and was very glad when I got this opportunity to take part in it. I felt like I was doing something for my dad by knowing more about the disease and giving him support." (Tseday Zewdu Tegegn)

"To even realize how far along I have come to understanding research and how a lab operates, I credit the experience that I have gained at CPDR, Center for Prostate Disease Research." (Zainab Afzal)

"This is the most exciting thing I have done in my education," (Henoke Shibeshi)

"It's not just about sitting in class and getting 4.0's. It's about getting out there to do the research and make the discoveries that will help people. (**Benjamin Ozokwere**)

Student Tracking and Extended Mentoring

The students trained under this program are in contact with the PD, Co-PIs, Mentors and to continue to interact and discuss their progress and guidance in choosing the appropriate career. Most of the students have chosen to continue education in obtaining graduate degree in biology or Medical sciences and related areas. The following is the list of the students and their status as of 2011:

Mr. Chiedozie Joseph Ayika: Graduated and working at the USUHS, applying to Nursing

School

Mr. Francisco Saenz: Graduated with Masters Degree in Cancer biology, Prevention and

Control. Currently working at Georgetown University Medical Center

Mr. Emmanuel Woode: Graduated and working with Misoscale Diagnostics,

Gaithersburg MD

Ms. Fitch Yelekal: Graduated and applying to Medical School

Ms. Zainab Afzal: Enrolled as Nursing and Biology Major at UDC

Ms. Emelia Daka: Enrolled Biology Major at UDC

Ms. Heran Kalyie: Graduated and applying to Medical School

Mr. Benjamin Ozokwere: Graduated and enrolled into Nursing School, UMDNJ, NJ

Mr. Henoke Shibeshi: Graduated and applying to Medical School

Ms. Tseday Tegegn: Enrolled as Biology Major at UDC

Ms. Preety Upadhyay: Graduated from UDC and currently a Registered Nurse

Ms. Nicola Eva Abdul: Enrolled as Nursing and Biology Major at UDC

Ms. Zainab Afzal: Enrolled as Nursing and Biology Major at UDC

Ms. Christelle Donfack: Graduated and working at UDC, applying for Graduate

School

Ms. Juliet Chijioke: Graduated and applying to Medical School

Mr. Habib Kedir: Enrolled as Biology and Chemistry Major at UDC

CONCLUSIONS:

Prostate cancer (CaP) is a major health concern for men in the USA with expected 217,730 new cases and 32,050 deaths in 2010. African American (AA) men have a 60% higher incidence rate and twice the death rate of white men, and it is the second leading cause of cancer-related death in AA men. Lack of minority research investigators has often been cited as one of the barriers to research addressing minority health issues, e.g., high CaP incidence in AA patients. Through the DoD-PCRP grant, USU-CPDR in partnership with UDC launched an educational effort to train minority students in prostate cancer research. The goal of the program is to increase the number of minority students pursuing careers in prostate cancer research.

During three years (2008-2010) of the grant, this collaboration has trained 16 meritorious UDC students who were selected after a rigorous selection by USU-CPDR and UDC selection committee. The students were assigned to the faculty members of USU who are focusing on specific research projects in CaP basic science and translational research in a multi-disciplinary setting involving cancer biologists, urologists, pathologists and biomedical informatics experts. These state-of-the-art projects represent high-impact research addressing CaP tumor biology, biomarkers, patient treatment and education. In addition to their project focus, students participated in weekly seminars presented by the USU-CPDR faculty and staff and guest speakers. This provided students the exposure to key issues in CaP research. Students prepared and presented their research goals and objectives and progress in biweekly presentations. At the end of the training, each student made presentations of the completed project in the form of a written report and a public seminar. The students also presented their research projects at the institutional and national meetings focusing the HBCU training and research. The program engaged prostate cancer researchers and students in mutually beneficial interactions resulting in a very rewarding experience for mentors as well as students in creating and maintaining a strong academic "pipeline" of students, who are likely to pursue professional career in medicine or bio-medical research. The excitement and success of this program is represented by training of 4 additional students than originally intended.

The HBCU summer training program between UDC and USU-CPDR has provided ground breaking unique opportunities for UDC students, who have expressed gratitude for this eye opening exposure and future commitment to professional training in prostate cancer research or similar biomedical research career.

During the training period, the students learned the following:

- Basic skills in planning and execution of a research project focused on a defined question related to molecular and cell biology of CaP or translational CaP research
- Presentation and development of a practical idea and its significance to CaP
- Importance of CaP research in high-risk populations, such as African Americans
- Preparation of high-quality slide presentations on assigned topics
- Maintenance of an electronic record of experiments and preparation of a final written report.
- Appreciation of the power of scientific research and its application in decreasing suffering from a disease such as cancer
- Appreciation of the dedication, perseverance, and effort it takes to perform research of the highest quality in a laboratory

REFERENCES:

None

APPENDICES:

Sur	porting	Data:
~~~	POLUM	

Summer Research Opportunity Announcement:	Attachment 1-3
CPDR/ USUHS News Releases: CPDR Receives Prostate Cancer Research Summer Internship Grant From DoD-PCRP:	Attachment 4-6
University of the District of Columbia Newsletters "Fire Bird"	Attachment 7, 8

**Summer Research Opportunity Announcements** 



## SUMMER RESEARCH OPPORTUNITY

Summer research opportunity is available at the Center for Prostate Disease Research (CPDR) at Uniformed Services University of Health Sciences (USUHS) on a UDC-CPDR jointly funded grant from the Department of Defense. The UDC-CPDR Summer Program provides a 12-week summer research experience in prostate cancer research for undergraduate students majoring in science, technology, engineering and mathematics (STEM) disciplines. The goal of this program is to prepare a diverse, highly talented, educated, and skilled pool of scientists in terested in Prostate Cancer Research. The students will be exposed to cutting edge research methods in prostate cancer. More information about CPDR can be found at <a href="http://www.cpdr.org">http://www.cpdr.org</a>

## **Eligibility**

- 1. The applicant must be a junior or senior at UDC when he/she returns to school in Fall 2008
- 2. Must be studying in STEM disciplines with an interest in Prostate Cancer Research.
- 3. Must have a cumulative GPA of 3.0 or above at the time of application.

#### **Stipend**

The participants to this program will receive a stipend @ \$10/hr, 40h/week for 12 weeks.

#### **Start Date**

June 1, 2008

## **Application**

Submit a letter of intent along with a short essay (1 page) on how this program will help you in achieving your career goals. The deadline for application is May15, 2008.

#### Submit your application to

## Dr. Deepak Kumar

Co-PI and Director of the UDC-CPDR Summer Research Program Department of Biological and Environmental Sciences University of the District of Columbia Building 44, Room 312 4200 Connecticut Avenue NW Washington DC 20008 Telephone: (202) 274-5937

Fax: (202) 274-5776 Email: dkumar@udc.edu



## 2009 SUMMER UNDERGRADUATE RESEARCH OPPORTUNITY

Summer research opportunity is ava ilable at the Center for Prostate Disease Research (CPDR), Uniform ed Services University (USU) of Health Sciences on a UDC-CPDR jointly funded program.

The Department of De fense, United States Army Me dical Research and Materi el Command (USAMRMC), awarded The Prostate Cancer Res earch Prog ram (PCR P) Collaborative Undergraduate Historically Black College And University Student Summer Training Program grant to the Uniformed Services University of the Health Sciences' (USU) Center for Prostate Disease Rese arch (CPDR) and the University of the District of Columbia (UDC) collaborative team.

A successful collaborative effort between Dr. Deepak Kumar, Department of Bi ological and Environmental Science, UDC, and Dr. Shiv Srivastava, Department of Surgery, USU/CPDR provides a great opportunity for talented UDC students to take part in this P rostate Cancer Training Program that is conducted during their summer break. The UDC-CPDR Summer Program provides a 12-week summer research experience in prostate cancer research for undergraduate students majoring in science, technology, engineering and m athematics (STEM) disciplines. The goal of this program is to prepare a diverse, highly talented, educated, and skilled pool of scientists interested in Prostate Cancer Research. The students will be exposed to cutting edge research methods in prostate cancer and will be mentored throughout their tenure at UDC. More inform ation about CPDR can be found at <a href="http://www.cpdr.org">http://www.cpdr.org</a>. Four (4) students will be selected for summer, 2009.

## **Eligibility**

- 1. The applicant must be a junior or senior at UDC when he/she returns to school in Fall 2009
- 2. Must be studying in STEM disciplines with an interest in Prostate Cancer Research.
- 3. Must have a cumulative GPA of 3.0 or above at the time of application.

#### **Stipend**

The participants to this program will receive a stipend @ \$10/hr, 40h/week for 12 weeks.

## **Start Date**

June 1, 2009

## **Application**

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#### Dr. Deepak Kumar

Co-PI and Director of the UDC-CPDR Summer Research Program

University of the District of Columbia

Department of Biological and Environmental Sciences; Building 44, Room 312

4200 Connecticut Avenue NW; Washington DC 20008

Telephone: (202) 274-5937; Fax: (202) 274-5776

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Summer research opp ortunity is available at the Center for Prostate Disease Research (CPDR) Uniformed Services University (USU) of Health Sciences on a UDC-CPDR jointly funded program.

The Departm ent of Defense, United States Army Medical Research and Materiel Command (USAMRMC), awarded The Prostate Cancer Research Program (PCRP) Collaborative Undergraduate Historically Black College And University Student Summer Training Program grant to the Uniformed Services University of the Health Sciences' (USU) Center for Prostate Disease Research (CPDR) and the University of the District of Columbia (UDC) collaborative team.

A successf ul collabo rative effort between Dr. D eepak Kum ar, Departm ent of Biological and Environmental Science, UDC, and Dr. Shiv Srivastava, Departm ent of Surgery, USU/CPDR provides a great opportunity for talented UDC students to take part in this Prostate Cancer Training Program that is conducted during their summ er break. The UDC-CPDR Summer Program provides a 12-week summer research experience in prostate cancer res earch for undergraduate students m ajoring in science, technology, engineering and mathematics (STEM) disciplines. The goal of this program is to prepare a diverse, highly talented, educated, and skilled pool of scientists interested in Prostate Cancer Research. The students will be exposed to cutting edge research methods in prostate cancer and will be mentored throughout their tenure at UDC. More information about CPDR can be found at <a href="http://www.cpdr.org">http://www.cpdr.org</a>. Four (4) students will be selected for summer, 2010.

#### **Eligibility**

- 1. The applicant must be a junior or senior at UDC when he/she returns to school in Fall 2010.
- 2. Must be studying in STEM disciplines with an interest in Prostate Cancer Research.
- 3. Must have a cumulative GPA of 3.0 or above at the time of application.

#### **Stipend**

The participants to this program will receive a stipend @ \$10/hr, 40h/week for 12 weeks.

#### **Start Date**

June 1, 2010

## **Application**

Submit a letter of intent along with a short essay (1 page) on how this program will help you in achieving your career goals. The deadline for application is April15, 2010.

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Email: dkumar@udc.edu

**CPDR/ USUHS News Releases** 



## **Uniformed Services University**

of the Health Sciences 4301 Jones Bridge Road Bethesda, MD 20814-4799

Release No.08-08-39

Aug. 11, 2008

**Contact:** Office of External Affairs **Voice:** 301-295-1219 Fax: 301-295-3757

Email: anicholson@usuhs.mil

News Release

# CPDR Receives Prostate Cancer Research Summer Internship Grant From DoD-PCRP

**BETHESDA, Md.** — The Prostate Cancer Research Program (PCRP) Collaborative Undergraduate Historically Black College And University Student Summer Training Program was awarded by the Department of Defense, United States Army Medical Research and Materiel Command (USAMRMC) to the Uniformed Services University of the Health Sciences' (USU) Center for Prostate Disease Research (CPDR) and the University of the District of Columbia (UDC) collaborative team.

A successful collaborative effort between Dr. Shiv Srivastava, Department of Surgery, USU/CPDR and Dr. Deepak Kumar, UDC, provides a great opportunity for talented students to take part in the new Prostate Cancer Training Program that is conducted during their summer break. Historically Black Colleges and Universities (HBCU) have a diverse student body with a majority of students classified as minorities. Health Disparities such as the higher incidence of prostate disease among African American men that have been the focus of the CPDR research team are increasingly being addressed in various diseases including prostate cancer. So what better way to increase awareness of such trends and move towards a cure than to:

- 1. Recruit and encourage highly qualified undergraduate trainees by providing them with a stimulating and intellectual environment that promotes state-of -the art training and education in prostate cancer research.
- 2. Motivate young researchers, who may contribute to prostate cancer research centers at HBCUs
- 3. Ensure that the new generation of biomedical scientists is properly trained to continue the fight against prostate cancer.

At the Uniformed Services University's Center for Prostate Disease Research (CPDR), the four selected summer students from UDC are paired with one of the faculty members of USU, and focus on specific research projects in basic science and database research. There are goals and objectives for both mentors and students. Students are actively involved in the program through progressive research, regular lab meetings, seminars and personal discussions with faculty members, staff and fellow students. Research findings are presented by the students, at the end of the summer experience aiming scientific publications. The National Conference Award provides a unique opportunity for gifted students in a leading institution of the prostate cancer field.

## Learning to Care for Those in Harm's Way

Located on the grounds of Bethesda's National Naval Medical Center and across from the National Institutes of Health, USU is the nation's federal school of medicine and graduate school of nursing. The university educates health care professionals dedicated to career service in the Department of Defense and the U.S. Public Health Service. Students are active-duty uniformed officers in the Army, Navy, Air Force and Public Health Service, who are being educated to deal with wartime casualties, national disasters, emerging infectious diseases, and other public health emergencies. Of the university's more than 4,000 physician alumni, the vast majority serve on active duty and are supporting operations in Iraq, Afghanistan, and elsewhere, offering their leadership and expertise.

For more information, contact the Office of External Affairs at 301-295-1219.

## Learning to Care for Those in Harm's Way



## **Uniformed Services University**

of the Health Sciences 4301 Jones Bridge Road Bethesda, MD 20814-4799

> Release No.09-09-30 November 9, 2009

**Contact:** Ken Frager, Office of External Affairs **Voice:** 301-295-3981 **Cell:** 240-281-2738

Email: kenneth.frager.ctr@usuhs.mil

## For Immediate Release:

## **Summer Internship Program Immerses Minority Students in Prostate Cancer Research**

The Uniformed Services University of the Health Sciences (USU) Center for Prostate Disease Research (CPDR) played host recently to seven students from the University of the District of Columbia for a rigorous twelve-week training internship focused on prostate cancer research.

The internship was established jointly by the CPDR, which is part of USU's Department of Surgery, and the University of the District of Columbia (UDC) in 2008 through a grant from the Department of Defense-Prostate Cancer Research Program (DoD-PCRP) and the United States Army Medical Research and Materiel Command (USAMRMC). The principal investigators of the grant are Shiv Srivastava, PhD, Co-Director of CPDR and Professor of Surgery and Deepak Kumar, PhD, Associate Professor, UDC. The program was coordinated by Taduru Sreenath, PhD, Assistant Director and the CPDR. Interns were selected based on academic achievements at UDC in prostate cancer research. CPDR provided a structured framework for the summer training program in a rich scientific environment that is credited for landmark discoveries in prostate cancer research.

The students presented the summary of their training and research accomplishments at USU to leaders from the participating organizations.

The presenters and the title of their concluding presentations were as follows:

- Emelia Daka, mentor: Albert Dobi, Ph.D.: "Defining mir-1271 in benign epithelial cells of tumor bearing prostate glands"
- Benjamin Ozokwere, mentor: Taduru Sreenath, Ph.D.: "Functional analysis of ERG oncogene and it's role in transdifferentiation"
- Heran Kalyie, mentor: Johnan Kaleeba, Ph.D.: "Human Herpes virus 8 in prostate cancer initiation and progression"
- Henoke Shibeshi, mentor: Meera Srivastava, Ph.D.: "Distinct tumor suppressor effects of wild type versus dominant negative Annexin 7 involve Fibroblast Growth Factor 8"
- Preety Upadhyay, mentor: Albert Dobi, Ph.D.: "ERG is a Transcriptional Repressor of Probasin Promoter (ARR2PB)"
- Tseday Zewdu Tegegn, mentor: Gyorgy Petrovics, Ph.D.: "Functional Analysis of ERG"
- Zainab Afzal, mentor: Shyh-Han Tan, Ph.D.: "Subcellular Localization and Transcriptional Activity of ERG Isoforms"

Located on the grounds of Bethesda's National Naval Medical Center and across from the National Institutes of Health, USU is the nation's federal school of medicine and graduate school of nursing. The university educates health care professionals dedicated to career service in the Department of Defense and the U.S. Public Health Service. Students are active-duty uniformed officers in the Army, Navy, Air Force and Public Health Service who are being educated to deal with wartime casualties, natural disasters, emerging infectious diseases, and other public health emergencies. Of the university's nearly 4,400 physician alumni and more than 400 advanced practice nurses, the vast majority serve on active duty and are supporting operations in Iraq,

Learning to Care for Those in Harm's Way

Afghanistan, and elsewhere, offering their leadership and expertise. The University also has graduated more than 600 public health professionals.

For more information about USU and its programs, visit www.usuhs.mil.

## Learning to Care for Those in Harm's Way



## **Uniformed Services University**

of the Health Sciences 4301 Jones Bridge Road Bethesda, MD 20814-4799

> Release No.10-08-60 August 31, 2010

**Contact:** Ken Frager, Office of External Affairs **Voice:** 301-295-3981 **Cell:** 240-281-2738

Email: kenneth.frager@usuhs.mil

## For Immediate Release:

## 2010 Internship Program Immerses Minority Students in Prostate Cancer Research

The Uniformed Services University of the Health Sciences (USU) Center for Prostate Disease Research (CPDR) recently completed its third consecutive summer internship program for outstanding students from the University of the District of Columbia (UDC). The program was established jointly in 2008 by the CPDR – part of USU's Department of Surgery – and the UDC, through a grant from the Department of Defense-Prostate Cancer Research Program (DoD-PCRP) award to Dr. Shiv Srivastava (PI), CPDR co-director and USU professor, and Dr. Deepak Kumar (Co-PI), Chair of the Department of Biology at UDC.

Five interns were selected for the 2010 program based on academic achievements at UDC in prostate cancer research. CPDR provided a structured framework for the program, offering a rich multi-disciplinary prostate cancer translational research environment that is credited for landmark discoveries. The students completed their program by presenting their training and research accomplishments at USU to leaders from the participating organizations. Dr. Taduru Sreenath, CPDR assistant director, served as the primary coordinator for the program.

#### The 2010 interns were:

- Nicola Abdul, mentor: Taduru Sreenath, Ph.D.: "TMPRSS2-Ets Related Gene Fusions in Mouse Model for Prostate Cancer"
- Zainab Afzal, mentor: Jane Hudak, RN, Ph.D.: "Shadowing Patients with Prostate Cancer"
- Juliet Chijioke, mentor: Hua Li, M.D., Ph.D.: "Regulation of Androgen Receptor Levels Through the PMEPA1-NEDD4-1 Feedback Loop"
- Christelle Donfack, mentor: Ahmed Mohamed, M.D., Ph.D.: "Characterization of ERG Protein in Prostate Cancer and Other Tumor Cell Lines"
- Habib Kedir, mentor: Gyorgy Petrovics, Ph.D.: "Urine Based Prostate Cancer Diagnostic Assay Development"

The Uniformed Services University of the Health Sciences (<a href="www.usuhs.mil">www.usuhs.mil</a>) is the nation's federal health sciences university. USU students are primarily active duty uniformed officers in the Army, Navy, Air Force and Public Health Service who are being educated to deal with wartime casualties, emerging infectious diseases and other public health emergencies. Of the university's more than 4,500 physician alumni, the vast majority are supporting operations in Iraq, Afghanistan and elsewhere, offering their leadership and expertise.

For more information about USU and its programs, visit www.usuhs.mil.

University of the District of Columbia Newsletters



#### **Fall Parking Permits**

On sale now

Park with peace of mind and avoid pesky tickets. Drive here for more details.

Late Registration

Tues., August 25

Classes Begin Wed., August 26

# Academic Enhancement Workshop for Students

August 27, 2:00 p.m.

Building 41, E-Lab 105
"Creating a Goal Plan"
The first 15 students to RSVP will be

selected to participate.
Email <u>ssstrong@udc.edu</u> or call

202.274.5526.

For the full listing of workshops click here

## Practical Nursing Program Pre-Entrance Exams

Fri., Aug. 28, & Sept. 4, 11, 9:30 a.m. 410 8th St., NW, Rm 304 Info: 202.274.6950

#### **Back to School BBQ**

Thurs., Sept 10, 12 -3 p.m. UDC Soccer Field For mouth-watering details email ceboa@udc.edu

- ★ Submission Request
- ★ Condolences

## August 21, 2009 — Internal Communications



Back: Zainab Afzal, Emelia Daka, Henoke Shibeshi, Benjamin Ozokwere, Dr. Tadaru Sreenat Front: Dr. Shiv Srivastava (CPDR), Tseday Zewdu Tegegn, Preety Upadhyay, Dr. Deepak Kumar (UDC) Absent: Heran Kalyle

#### **UDC Students Make Significant Contributions to Cancer Reasearch**

On August 14, seven UDC undergraduates along with a University of Pittsburgh student presented the results of their summer prostate cancer research. They worked in research laboratories, mentored by several researchers at the Center for Prostate Disease Research at USU in Bethesda. In many cases, the students' results represent significant discoveries with potential impact for the diagnosis or treatment of prostate cancer. "This is the most exciting thing I have done in my education," Henoke Shibeshi concluded. While Ben Ozokwere said, "It's not just about sitting in class and getting 4.0's. It's about getting out there to do the research and make the discoveries that will help people." Nursing major, Preety Upadhyay said, "It's a very big deal for me," while Emilia Daka reported "It was my first ever research program and I had a lovely time. I have learned a lot."

The HBCU Summer Undergraduate Training Program in Prostate Cancer Research is funded by a grant from the Department of Defense. Dr. Shiv Srivastava in the Department of Surgery at USU and Dr. Deepak Kumar in the UDC Department of Biological and Environmental Sciences are the co-principal investigators. One of the UDC students was funded by the STEM Center grant from the National Science Foundation, directed by Dr. Freddie Dixon, department chairperson for Biological and Environmental Sciences.

## **Multi-Institution Distance Learning Option for Fall**

Do you need a university-wide social science requirement? Do you want to be part of a nation-wide learning community? Do you want to interact and talk to leading politicos in a synchronous interview format with C-SPAN and other institutions? Then you need to enroll in the distance learning course **Bureaucracy and Policy Making** (1169-346) being held on Thursdays from 2 p.m. - 5 p.m. The course studies the role of bureaucracies in policy-making and their interactions with the other elements of the political system. Discuss such topics as the sources of bureaucratic power, the bureaucratic policy process, and the interactions of bureaucracy with the executive, legislative, non-governmental structure, and the public.

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# University of the District of Columbia

**UDC News** 

August 24, 2010

#### FOR IMMEDIATE RELEASE

#### **UDC Students Make Significant Contributions to Prostate Cancer Research**



Front: Shiv Srivastava (CPDR), Habib Kedir (junior in biology and chemistry), Juliet Chijioke (junior in biology), Deepak Kumar (UDC faculty), Christelle Donfack (junior in biology), Tadaru Sreenath(CPDR), Tseday Z. Tegegn (junior in biology).

Back: Albert Dobi (CPDR), Gyorgy Petrovics(CPDR), Zainab Afzal (junior in biology and nursing), Nicola Abdul (sophomore in nursing), David G. McLeod (CPDR), Ahmed Mohamed(CPDR).

**Washington, DC** - Five UDC undergraduates spent summer 2010 doing research to improve the prognosis of prostate cancer - the number one non-skin cancer affecting US men, and the number two cancer killer of men. Mentored by researchers at the Center for Prostate Disease Research (CPDR) at the Uniformed Services University Health Sciences campus in Bethesda, Maryland, the students presented their results at a symposium on August 18, 2010. In some cases, the students' results represent significant, unanticipated discoveries with potential benefits for the diagnosis or treatment of prostate cancer. "We are doing this for the cancer patients," said Dr. Shiv Srivastava (CPDR), co-Director of the research program with UDC biology chairperson, Dr. Deepak Kumar. At CPDR, the program was coordinated by Dr. Taduru Sreenath.

"I learned a lot, a lot, a lot about research," said junior biology/nursing major, Zainab Afzal, a sentiment echoed by the others. The HBCU Summer Undergraduate Training Program in Prostate Cancer Research is funded by a grant from the Department of Defense to Drs. Srivastava (CPDR) and Kumar (UDC). The students look forward to presenting their research at major national conferences in the fall.

The UDC students worked on the following topics, using state-of-the-art techniques, including immunofluorescence microscopy, gain and loss of function studies utilizing adenovirus and siRNA based approaches, analyzing signaling proteins by Western Blotting and immunohistochemistry.

Ms. Zainab Afzal (Junior Biology and Nursing Major): Shadowing Patients with Prostate Cancer (mentor: Dr. Jane Hudak)

Mr. Habib Kedir (Junior Biology and Chemistry Major): Urine Based Prostate Cancer (mentor: Dr. Gyorgy Petrovics)

Diagnostic Assay Development Ms. Juliet Chijioke (Junior Biology Major): Regulation of Androgen Receptor Levels through the PMEPA1-NEDD4-1 Feedback Loop (mentor: Dr. Shyh-Han Tan)

Ms. Christelle Donfack (Junior Biology Major): Characterization of ERG Protein in Prostate Cancer and other Tumor Cell Lines (mentor: Dr. Ahmed Mohamed)

Ms. Nicola Abdul(Sophomore Nursing Major): TMPRSS2-Ets Related Gene Fusions in Mouse Model for Prostate Cancer (mentor: Dr. Taduru Sreenath)

According to the National Cancer Institute, about 218,000 American men are expected to be diagnosed with prostate cancer in 2010, and prostate cancer will result in 32,000 deaths in 2010. African American men have a 60% higher incidence rate and twice the death rate from prostate cancer, compared with white men.

